

Claims 12-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Belkowski, S.M. (1991). The Office Action states that Belkowski teaches the use of a combination of dimethylglycine and a *Perna canaliculus* component for the treatment of an inflammatory disease. The Office Action acknowledges that Belkowski does not teach the claimed invention in that it does not teach a composition of dimethylglycine and a *Perna canaliculus* component administered together and in that it does not teach a kit comprising a composition of dimethylglycine and a *Perna canaliculus* component. However, the Office Action states that it would have been *prima facie* obvious to one of ordinary skill in the art to combine dimethylglycine and a *Perna canaliculus* component, as taught by Belkowski, in a single mixture for convenience, and to place said compositions in a kit for convenience.

However, there is no suggestion in Belkowski that dimethylglycine or a *Perna canaliculus* component be combined in single composition or as components of a kit. Belkowski does disclose the experimental testing of both a *Perna canaliculus* component, and a combination of a *Perna canaliculus* component and dimethylglycine, for their effects on the development of collagen induced arthritis in rats. However, as clearly shown in Table 3.1 on page 61 of the Belkowski article, combining the administration of dimethylglycine with the administration of a *Perna canaliculus* component did not provide any added benefits to those achieved with a *Perna canaliculus* component alone. For example, results achieved in terms of both "Percentage of Arthritic Animals" and "Average Paw Size" were better when a *Perna canaliculus* component was used alone versus when a *Perna canaliculus* component was used in combination with dimethylglycine. Additionally, the results achieved in terms of "Average Day of Occurrence" were comparable when a *Perna canaliculus* component was used in combination with dimethylglycine or when a *Perna canaliculus* component was used alone. Therefore, as a whole, the Belkowski reference actually teaches away from the combination of a *Perna canaliculus* component with dimethylglycine for the treatment of arthritic disease, rather than suggesting the combination of the two components.

Claims 12-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kendall (U.S. Patent No. 5,026, 728), in view of Caughey et al. (1983) or Gibson et al. (1980) or McFarlane (U.S. Patent No. 4,455,298).

The Office Action acknowledges that the cited references do not teach a combination of dimethylglycine with a *Perna canaliculus* component, either as a composition or kit. However, the Office Action states that it would have been obvious to one of ordinary skill in the art to combine, in a composition, the anti-inflammatory compound dimethylglycine, as taught by Kendall et al., with an anti-inflammatory compound/composition of *Perna canaliculus*, as taught by Caughey, Gibson, or the '298 patent. However, in arriving at this rejection, the Examiner fails to use the prior art as a whole, and impermissibly uses hindsight and Applicants invention as the suggestion for combining the references. *In re Gorman*, 18 USPQ2d 1885 (Fed. Cir. 1991). For example, the Belkowski reference discussed above actually teaches away from the use of a combination of dimethylglycine and a *Perna canaliculus* component for the treatment of an inflammatory disease. Therefore, in considering the prior art as a whole, one of skill in the art would not be motivated to make the combination, as suggested by the Examiner.

However, assuming *arguendo* that a *prima facie* case of obviousness for combining dimethylglycine and a *Perna canaliculus* component has been established, Applicants have demonstrated unexpected results for the dimethylglycine/*Perna* combination in the instant application. Specifically, as stated on page three of the application, Applicant's have discovered that dimethylglycine and *Perna* have a synergistic effect in the treatment of inflammatory disease, particularly in the treatment of autoimmune disease. In this regard, Applicant's point out the data in Example 2 of the instant application, wherein it is demonstrated that combination of dimethylglycine and a *Perna canaliculus* component showed a synergistic effect in reducing the number of anti-single stranded DNA antibodies and anti-double stranded DNA antibodies, hallmarks for lupus erythmatosus, in a murine model of lupus erythmatosus. Furthermore, the dimethylglycine/*Perna* combination showed synergistic effects in altering the immune profiles in the mice. For example, as described in Example 2, dimethylglycine/*Perna* treated animals showed significantly lower levels of serum il-10 than either control animals or animals treated with dimethylglycine or *Perna* alone, thus indicating a shift from a Th2 response to a Th1 response, with a concomitant decrease in excess antibody production, including anti-nuclear antibody production. Thus, Applicants maintain that the combination of dimethylglycine and a *Perna canaliculus* component, either combined in the form of a composition or kit, are not

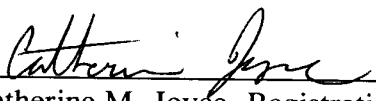
obvious over the prior art. Applicants will supply a declaration directed to these disclosed unexpected results if necessary. Applicants respectfully request that the rejection of claims 12-18 as obvious over the prior art be withdrawn.

New Claims

New claim 19 was added to specify a kit according to claim 15, wherein the dimethylglycine formulation is suitable for oral administration. Support for new claim 19 may be found in the specification on page 8, lines 1-5.

The claims of the application are believed to be in condition for allowance. However, the examiner is cordially invited to telephone the undersigned at the number below with any questions or comments.

Respectfully submitted,


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